Complete Summary

GUIDELINE TITLE

EFNS guidelines on neurostimulation therapy for neuropathic pain.

BIBLIOGRAPHIC SOURCE(S)

Cruccu G, Aziz TZ, Garcia-Larrea L, Hansson P, Jensen TS, Lefaucheur JP, Simpson BA, Taylor RS. EFNS guidelines on neurostimulation therapy for neuropathic pain. Eur J Neurol 2007 Sep;14(9):952-70. [53 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Neuropathic pain

GUIDELINE CATEGORY

Management
Technology Assessment
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine

Neurology
Physical Medicine and Rehabilitation

INTENDED USERS

Occupational Therapists
Physical Therapists
Physicians

GUIDELINE OBJECTIVE(S)

To provide the neurologist with evidence-based recommendations that may help to determine when a patient with neuropathic pain should try a neurostimulation procedure

TARGET POPULATION

Patients presenting with neuropathic pain

INTERVENTIONS AND PRACTICES CONSIDERED

1. Peripheral stimulation including transcutaneous electrical nerve stimulation (TENS), peripheral nerve stimulation (PNS), and nerve root stimulation (NRS)
2. Spinal cord stimulation (SCS)
3. Deep brain stimulation (DBS)
4. Motor cortex stimulation (MCS)
5. Repetitive transcranial magnetic stimulation (rTMS)

MAJOR OUTCOMES CONSIDERED

Effectiveness of neurostimulation therapy in terms of pain relief and quality of life

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Search Methods

Task Force participants were divided into subgroups and assigned the search for specific neurostimulation procedures, with two persons carrying out an independent search for each procedure. A two-stage approach to the relevant literature search was undertaken. First the MEDLINE, EMBASE, and Cochrane databases were searched for systematic reviews, from inception date to May

2006. Detailed searches are listed in Appendix 1 (see "Supplementary Material" in the original guideline document).

Recent textbooks known to the authors were also examined for relevant references. These reviews and books were used to identify the primary literature. Secondly, given the search cut off dates of previous systematic reviews, an update search for primary studies (randomized controlled trials, nonrandomized controlled trials, observational comparative studies, and case series) was undertaken. Studies identified by this updated search were added to the body of evidence for each neurostimulation procedure under each indication heading.

All study designs were included except case reports and very small case series (<8). In addition, Task Force participants excluded those multiple-indication case series without disaggregated reported outcomes. Both reviewers undertook the study selection. For each indication, the number and type of studies was indicated and a summary of efficacy and harm findings given. Where there was more than one systematic review or primary publication on the same series of patients, the most comprehensive analysis was taken.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Evidence Classification Scheme for a Therapeutic Intervention

Class I: An adequately powered prospective, randomized, controlled clinical trial with masked outcome assessment in a representative population or an adequately powered systematic review of prospective randomized controlled clinical trials with masked outcome assessment in representative populations. The following are required:

a. Randomization concealment
b. Primary outcome(s) is/are clearly defined
c. Exclusion/inclusion criteria are clearly defined
d. Adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias
e. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences

Class II: Prospective matched-group cohort study in a representative population with masked outcome assessment that meets a–e above or a randomized, controlled trial in a representative population that lacks one criteria a–e

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment

Class IV: Evidence from uncontrolled studies, case series, case reports, or expert opinion

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The evidence was graded and a recommendation for each indication applied according to the European Federation of Neurological Societies (EFNS) guidelines (see the "Rating Scheme for the Strength of the Evidence" and the "Rating Scheme for the Strength of the Recommendations" fields). The full list of references of all the assessed studies can be found in Appendix 2 (see "Supplementary Material" in the original guideline document).

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Rating of Recommendations for a Therapeutic Intervention

Level A rating (established as effective, ineffective, or harmful) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (probably effective, ineffective, or harmful) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (possibly effective, ineffective, or harmful) requires at least two convincing class III studies.

COST ANALYSIS

A published cost analysis was reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guidelines were validated according to the European Federation of Neurological Societies (EFNS) criteria (see the "Availability of Companion Documents" field in this summary).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of evidence (class I-IV) supporting the recommendations and ratings of recommendations (A-C) are defined at the end of the "Major Recommendations" field.

Peripheral Stimulations (Transcutaneous Electrical Nerve Stimulation [TENS], Peripheral Nerve Stimulation [PNS], and Nerve Root Stimulation [NRS])

The guideline developers cannot draw any conclusion for PNS and NRS. Even for TENS, it is difficult to come to conclusive recommendations. The total number of patients with ascertained neuropathic pain was only some 200, with diseases, comparators, and results varying considerably from study to study. Stimulation parameters also vary considerably between the studies, using different pulse waveforms and a wide range of frequencies, not to mention number and duration of the sessions. In conclusion, standard high-frequency TENS is possibly better than placebo (**level C**) though probably worse than acupuncture-like or any other kind of electrical stimulation (**level B**).

Refer to Table 1 in the original guideline document for summary of efficacy and safety of peripheral stimulations.

Spinal Cord Stimulation (SCS)

The guideline developers found **level B** evidence for the effectiveness of SCS in failed back surgery syndrome (FBSS) and complex regional pain syndrome, type I (CRPS I). The available evidence is also positive for CRPS type II, peripheral nerve injury, diabetic neuropathy, post-herpetic neuralgia (PHN), brachial plexus lesion, amputation (stump and phantom pains), and partial spinal cord injury, but still requires confirmatory comparative trials before the use of SCS can be unreservedly recommended in these conditions.

Refer to Table 2 in the original guideline document for summary of efficacy and safety of SCS.

Deep Brain Stimulation (DBS)

For the use of DBS there is weak positive evidence in peripheral neuropathic pain including pain after amputation and facial pain (expert opinion requiring confirmatory trials). In central post-stroke pain (CPSP), DBS results are equivocal and require further comparative trials.

Refer to Tables 3, 4, 5, and 6 in the original guideline document for summary of efficacy and safety of DBS.

Motor Cortex Stimulation (MCS)

There is **level C** evidence (two convincing class III studies, 15 to 20 convergent class IV series) that MCS is useful in 50 to 60% of patients with CPSP and central or peripheral facial neuropathic pain, with small risk of medical complications. The evidence about any other condition remains insufficient.

Refer to Tables 7 and 8 in the original guideline document for summary of efficacy and safety of MCS in CPSP and facial pain, respectively.

Repetitive Transcranial Magnetic Stimulation (rTMS)

There is moderate evidence that rTMS of the motor cortex, using a figure-of-eight coil and high frequency (5 to 20 Hz) induces significant pain relief in CPSP and several other neuropathic pain conditions (**level B**). However, because the effect is modest and short-lasting, rTMS should not be used as the sole treatment in chronic neuropathic pain. It may be proposed for short-lasting pains or to identify suitable candidates for an epidural implant (MCS). In contrast, in the same pain conditions, low-frequency rTMS is probably ineffective (**level B**).

Refer to Tables 9 and 10 in the original guideline document for summary of efficacy and safety of rTMS.

Definitions:

Evidence Classification Scheme for a Therapeutic Intervention

Class I: An adequately powered prospective, randomized, controlled clinical trial with masked outcome assessment in a representative population or an adequately powered systematic review of prospective randomized controlled clinical trials with masked outcome assessment in representative populations. The following are required:

a. Randomization concealment
b. Primary outcome(s) is/are clearly defined
c. Exclusion/inclusion criteria are clearly defined
d. Adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias
e. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences

Class II: Prospective matched-group cohort study in a representative population with masked outcome assessment that meets a–e above or a randomized, controlled trial in a representative population that lacks one criteria a–e

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment

Class IV: Evidence from uncontrolled studies, case series, case reports, or expert opinion

Rating of Recommendations >for a Therapeutic Intervention

Level A rating (established as effective, ineffective, or harmful) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (probably effective, ineffective, or harmful) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (possibly effective, ineffective, or harmful) requires at least two convincing class III studies.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for selected recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of neurostimulation therapy for neuropathic pain

POTENTIAL HARMS

Adverse Effects of Neurostimulation Therapy

- *Spinal cord stimulation (SCS)*: In a pooled safety analysis of SCS across all indications, the undesired events were mostly dysfunction in the stimulating apparatus: lead migration (13.2%), lead breakage (9.1%), and other minor hardware problems. Also the medical complications were minor and never life threatening and were usually solved, like the hardware problems, by removing the device. The overall infection rate was 3.4%.
- *Deep brain stimulation (DBS)*: Wound infection, lead fractures, intra-operative seizure, and post-operative burr hole site erosion were observed.
- *Motor cortex stimulation (MCS)*: Most common undesired events were related to some malfunction of the stimulating apparatus (e.g., unexpected battery

depletion). Seizures, wound infection, sepsis, extradural haematoma, and pain induced by MCS have also been reported.

General Comments

Concerning harms, transcutaneous electrical nerve stimulation (TENS) and repetitive transcranial magnetic stimulation (rTMS) are virtually harmless. SCS, DBS, and MCS do entail adverse events in a large proportion of patients (up to 20% with MCS and 40% with SCS experience one or more complications. However, most of the complications are simple lead migration or battery depletion that do not produce physical harm and can usually be solved. Real harms are few, usually wound infection (3.4% with SCS, 7.3% with DBS, and 2.2% with MCS) and very rare cases—often single cases—of aseptic meningitis, transient paraparesis, epidural haematoma, epileptic seizures and skin reactions, none being life-threatening. There was only one case of pre-operative death 20 years ago.

Refer to Tables 1, 2, 4, and 7 through 10 for additional information on adverse effects of neurostimulation therapy.

CONTRAINDICATIONS

CONTRAINDICATIONS

Contraindications for deep brain stimulation include psychiatric illness, uncorrectable coagulopathy, and ventriculomegaly precluding direct electrode passage to the surgical target.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This guideline provides the view of an expert task force appointed by the Scientific Committee of the European Federation of Neurological Societies (EFNS). It represents a peer-reviewed statement of minimum desirable standards for the guidance of practice based on the best available evidence. It is not intended to have legally binding implications in individual cases.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The European Federation of Neurological Societies has a mailing list and all guideline papers go to national societies, national ministries of health, World Health Organisation, European Union, and a number of other destinations. Corporate support is recruited to buy large numbers of reprints of the guideline papers and permission is given to sponsoring companies to distribute the guideline papers from their commercial channels, provided there is no advertising attached.

IMPLEMENTATION TOOLS

Staff Training/Competency Material

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Cruccu G, Aziz TZ, Garcia-Larrea L, Hansson P, Jensen TS, Lefaucheur JP, Simpson BA, Taylor RS. EFNS guidelines on neurostimulation therapy for neuropathic pain. Eur J Neurol 2007 Sep;14(9):952-70. [53 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2007 Sep

GUIDELINE DEVELOPER(S)

European Federation of Neurological Societies - Medical Specialty Society

SOURCE(S) OF FUNDING

European Federation of Neurological Societies

GUIDELINE COMMITTEE

European Federation of Neurological Societies Panel on Neuropathic Pain

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Task Force Members: G. Cruccu, Department of Neurological Sciences, La Sapienza University, Roma, Italy; T. Z. Aziz, Oxford Functional Neurosurgery, Department of Neurosurgery, Radcliffe Infirmary, Oxford, UK; L. Garcia-Larrea, INSERM 'Central integration of pain' (U879) Bron, University Lyon 1, France; P. Hansson, Department of Neurosurgery, Pain Center, Karolinska University Hospital and Pain Section, Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden; T. S. Jensen, Danish Pain Research Center, Aarhus University Hospital, Aarhus, Denmark; J. P. Lefaucheur, Department of Physiology, Henri Mondor Hospital, AP-HP, Creteil, France; B. A. Simpson, Department of Neurosurgery, University Hospital of Wales, Heath Park, Cardiff, UK; R. S. Taylor, Peninsula Medical School, Universities of Exeter & Plymouth, UK

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

RST has a consultant contract with Medtronic, as an expert in Health Care Policy and Clinical Trial Design. PH, LGL, JPL, and BS received honorarium from Medtronic for lectures or advisory boards. The other authors have nothing to declare.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available to registered users from the European Federation of Neurological Societies Web site.

Print copies: Available from Dr G. Cruccu, Dipartimento Scienze Neurologiche, Viale Università 30-00185 Roma, Italy (tel.: +39 06 49694209; fax: +39 06 49314758; e-mail: cruccu@uniroma1.it).

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Brainin M, Barnes M, Baron JC, Gilhus NE, Hughes R, Selmaj K, Waldemar G; Guideline Standards Subcommittee of the EFNS Scientific Committee. Guidance for the preparation of neurological management guidelines by EFNS scientific task forces – revised recommendations 2004. Eur J Neurol. 2004 Sep;11(9):577-81. Electronic copies: Available from the European Federation of Neurological Societies Web site.
- Guideline papers. European Federation of Neurological Societies. Electronic copies: Available from the European Federation of Neurological Societies Web site.
- Continuing Medical Education questions available from the European Journal of Neurology Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on October 15, 2007.

COPYRIGHT STATEMENT

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion.aspx .

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

Date Modified: 10/13/2008


DEPARTMENT OF HEALTH & HUMAN SERVICES • USA